Technoleg Iechyd Cymru
Health Technology Wales

HEALTH TECHNOLOGY WALES (HTW) EVIDENCE SUMMARY 021
(September 2020)

Point-of-care haemolysis detection

HTW Assessment Group decision

HTW undertook an evidence review to address the following question: is point-of-care haemolysis detection in secondary care clinically and cost effective in comparison to haemolysis detection in central laboratories?

The evidence identified was judged to be of limited applicability to decision makers. There was a lack of sufficient evidence on the utility of the test particularly in relation to how its use influences the need for re-sampling, and time taken for re-sampling, when blood tests are taken and haemolysis is present.

The HTW Assessment Group concluded that there is currently insufficient evidence on point-of-care haemolysis detection to inform the production of Guidance at this time. Therefore, this topic will not progress to Appraisal Panel and will not receive HTW Guidance recommendations.

Why did HTW appraise this topic?

Haemolysis is the release of haemoglobin and other intracellular components from red blood cells into the surrounding plasma following damage or disruption to the cell membrane. Haemolysis has been shown to introduce a meaningful bias in several blood gas and electrolyte parameters. Clinicians therefore run the risk of basing clinical decisions on erroneous data due to haemolysis, which can lead to adverse events.

Point-of-care testing enables healthcare personnel to test blood for haemolysis directly at the patient's side. Hemcheck Sweden AB's CE-marked, patented Helge product consists of two different disposable tests: the s-test for blood gas syringe samples and the v-test for test tube samples; and a common digital reader that determines whether the blood sample is haemolysed or not.

Evidence Summary

HTW identified one non-randomised, open-label, comparative trial, which reported that that the Helge point-of-care haemolysis s-test has the potential to detect haemolysis with a sensitivity of 80% and a specificity of 99%, at a haemoglobin concentration cut-off of 0.5 grams per litre; and a sensitivity of 84.8% and specificity of 99.9%, at a haemoglobin concentration cut-off of 1 gram per litre. An unpublished conference poster showed that that the proportion of laboratory-

rejected samples would be reduced in those samples tested using the Helge v-test compared to those not pre-tested.

The single published study was conducted in the emergency department of a Swedish hospital, and may therefore be of limited in Welsh practice. No evidence was identified about how point-of-care haemolysis detection influences the time required for sample analysis, changes in requirement for re-sampling/ability to re-sample using the original puncture site, or patient satisfaction.

A cost-benefit analysis suggests that point-of-care haemolysis testing is associated with a net cost reduction, but this reduction is highly dependent on the prevalence of haemolysis in samples and the cost of delayed resampling, both of which could not be estimated with certainty.

Evidence Appraisal Report 021 follows, and gives a full report of the evidence on this topic.

Technoleg Iechyd Cymru
Health Technology Wales

Evidence Appraisal Report

Point-of-care haemolysis detection

1. Purpose of the evidence appraisal report

This report aims to identify and summarise evidence that addresses the following question: is point-of-care haemolysis detection in secondary care clinically and cost effective in comparison to haemolysis detection in central laboratories?

Evidence Appraisal Reports are based on rapid systematic literature searches, with the aim of published evidence identifying the best clinical and economic evidence on health technologies. Researchers critically evaluate this evidence. The draft Evidence Appraisal Report is reviewed by experts and by Health Technology Wales multidisciplinary advisory groups before publication.

2. Health problem

Haemolysis is the release of haemoglobin and other intracellular components from red blood cells into the surrounding plasma following damage or disruption to the cell membrane (Lippi et al. 2008). Haemoglobin released from red blood cells in the plasma is referred to as free haemoglobin (Azhar et al. 2019). Haemolysis may occur within the body (in vivo), due to immunological or genetic disorders, infections and certain medicines; and/or during or after blood collection (in vitro). Inappropriate phlebotomy practices, sample processing techniques, improper sample storage and transportation conditions are the main contributors to in-vitro haemolysis (Azhar et al. 2019). Up to 98% of haemolysis is due to in vitro haemolysis (Lippi et al. 2008). The European Federation of Clinical Chemistry and Laboratory Medicine&COLABIOCLI (2018) produced recommendations to minimise the risk of haemolysis in venous blood sampling.

Laboratory testing provides essential information used by clinicians in medical decision-making (Green 2013). The majority of laboratory test errors occur in the pre-analytical phase (all of the steps from the time of test-ordering by the clinician until the sample is ready for analysis) (Green 2013), with haemolysis being one of the leading causes of pre-analytical laboratory errors (McCaughey EJ et al. 2016). Research suggests that accident and emergency (A&E) departments are major contributors of haemolysed specimens compared to other wards (Lippi et al. 2011). Prevalence of haemolytic specimens has been reported to be around 3.3% of all routine samples sent to clinical laboratories (Carraro P et al. 2000, Lippi et al. 2008).

Haemolysis has been shown to introduce a meaningful bias in several blood gas and electrolyte parameters, including partial pressure of oxygen, partial pressure of carbon dioxide, calcium and potassium (Lippi&Plebani 2013). Clinicians therefore run the risk of basing clinical decisions on

erroneous data due to haemolysis, which can lead to adverse events. The amount of haemolysis needed to affect a test is dependent on the test being performed. In general, slight haemolysis has little effect on most tests; however, it will cause falsely elevated levels for specific tests like potassium and lactate dehydrogenase (Calgary Laboratory Services 2020). Abnormalities in potassium levels are common in critically ill people, such as those in A&E departments and intensive care units, and might be life-threatening. Haemolysis can potentially lead to incorrect diagnoses when present in these situations (Wilson A et al. 2018). Grossly haemolysed samples can affect the results of many tests; therefore, a recollection will be requested for most grossly haemolysed samples (Calgary Laboratory Services 2020).

3. Health technology

Point-of-care testing (POCT), also known as near-patient testing, for haemolysis enables healthcare personnel to test blood for haemolysis directly at the patient's side. Current clinical practice in Wales involves two main methods of blood sample collection in primary and secondary care:

- Blood gas syringe samples are analysed at point-of-care (POC) using blood gas analysers, which currently do not have haemolysis-detection capabilities.
- Test tubes containing blood samples are sent to central laboratories for analysis. Laboratory equipment usually involves an automated detection system using the haemolysis index. The haemolysis index is a calculation, based on absorbance measurements performed on blood serum or plasma at different wavelengths, which provides a semi-quantitative estimate of haemolysis detected in the sample (Dolci A&Panteghini M 2014, Simundic AM et al. 2009).

Hemcheck Sweden AB's CE-marked, patented Helge product consists of two different disposable tests: the s-test for blood gas syringe samples and the v-test for test tube samples; and a common digital reader that determines whether the blood sample is haemolysed or not. The reader is mobile and can sit on a trolley or next to a blood gas analysis instrument. At the time of writing this report, the device cannot be connected to a blood gas analyser: the result from the haemolysis test is manually inputted into the blood gas analyser. The dispensing technique is the only methodological difference between these two tests.

Helge is used by adding a small amount of blood to the disposable test device, where the plasma or serum is separated from whole blood by vertical and lateral flow filtration. The disposable test is then placed in the digital reader, which photometrically analyses the colour of the plasma or serum. The camera sensor in the reader is made up of a matrix of light sensors, and the signal from each red, green and blue light sensor is combined into one value, which is correlated to a haemoglobin concentration. The haemoglobin concentration is translated to a haemolytic index, 0 to 555, with one haemolytic index unit equivalent to 0.01 grams per litre (g/L) (one milligram per decilitre [mg/dL]). It takes a few seconds for the blood to be analysed for haemolysis. The user can pre-define which value should be considered positive for haemolysis. The reader executes replicate measurements of a sample to optimise the precision. If the measurement is close to the cut-off value, the number of replicate measurements increases.

If deemed non-haemolysed, the blood samples from the test tubes can be sent to the central laboratory for analysis. If the sample is deemed haemolysed, additional samples of blood can directly be taken and checked for haemolysis. For blood gas syringes, the blood can be checked for haemolysis using the s-test before or after the blood is inserted into the blood gas analyser.

The Helge reader is not sensitive to some types of interference in blood samples: high levels of bilirubin increases the risk of false-negative haemolysis results, and high haematocrit blood samples have an increased risk of false-positive haemolysis results.

4. Evidence search methods

The Population-Intervention-Comparator-Outcomes framework for the evidence appraisal (Appendix 1) was developed following input from the Health Technology Wales (HTW) Assessment Group and UK experts.

A systematic literature search was undertaken on 9, 28 and 29 January 2020. Databases searched included Medline, Embase, Cochrane Library and Epistemonikos. Identified studies were only included if diagnostic outcomes of POC haemolysis detection were reported in a clinical setting. Appendix 2 summarises the selection of articles for inclusion in the review.

5. Clinical effectiveness

Blood collected in blood gas syringes

Our literature search identified one relevant study investigating haemolysis POCT; this same study was also highlighted to us by the Topic Proposer. This study was a non-randomised, comparative trial which met the inclusion criteria for this review and reported diagnostic accuracy (Duhalde et al. 2019). The study only looked at blood gas syringe samples (s-test) for POC haemolysis detection and not the test tube samples (v-test). The design of the study is summarised in Table 1.

Table 1. Study characteristics

Study design	Participants	Interventions	Outcomes	Comments
Non-randomised, open-label, method comparison between POC haemolysis detection system and routine haemolysis detection in central laboratory Single centre (emergency department in Swedish hospital)	1,270 blood samples from patients in an emergency department, taken by both physicians and nurses, were successfully analysed. Thirty-four samples were excluded due to missing data from the Department of Clinical Chemistry, and three samples were excluded due to errors in POC analysis. Exclusion criterion: less than 300 microlitres of blood in sample.	Index test: Helge H10 s-system for POC haemolysis detection (using blood gas syringe samples only, and not test tubes). Haemolysis measurement was performed directly after blood gas analysis. Blood gas analysis was done using an ABL800 FLEX (Radiometer, Copenhagen, Denmark). Samples where the POC method measured a free haemoglobin value of more than 0.3 g/L (30 mg/dL) were considered close to the clinical cut-off (0.5 g/L [50 mg/dL]). These cases were analysed further with more detailed continuous data from the reference method to ensure that the POC method and the reference method results were on the same side of the clinical cut-off. Reference standard: The remaining 200 (+) microlitres of the original sample was aliquoted to an Eppendorf tube and centrifuged. One hundred microlitres of the resulting plasma was aliquoted to another Eppendorf tube, and samples were transported to a central laboratory where haemolysis was measured using the Beckman Coulter AU680 Analyser (central laboratory detection). This technology analyses haemolysis semi-quantitatively using wavelengths to calculate the haemolysis index. In addition to this, a visual assessment was made by three independent operators.	Proportion of haemolytic blood gas samples in arterial and venous blood gas samples Levels of haemolysis detection in the POC device compared to routine central laboratory method. For both the index test and reference standard, haemolysis was defined as more than 0.5 g/L (50 mg/dL) of free haemoglobin in plasma. Outcomes were also measured using a cut-off of 1 g/L (100 mg/dL) of free haemoglobin in plasma.	Of the 1,270 blood samples analysed, 95% were venous, 3% arterial and 2% were unknown. Haemolysis was present in 9.5% of the 42 arterial blood samples. Source of funding not stated, but two out of three study authors are employees of Hemcheck, the Technology Developer.

g/L: grams per litre; POC: point-of-care; mg/dL: milligrams per decilitre

Blood collected in test tubes

An unpublished conference poster provides information on a method comparison study of POC haemolysis-detection in vacuum tubes (Helge v-test). The study took place in an emergency department of a Swedish hospital and 794 venous blood samples were collected in lithium heparin tubes. After being tested using the POC device, samples were sent to the central laboratory for testing by the reference method (Vitros 5.1 FS and 6500).

Health Technology researchers also identified a press release which describes the effect on haemolysis detection using Hemcheck's Helge product for test tubes (v-test). The study included 758 blood samples (Hemcheck Sweden AB 2020).

5.1 Clinical outcomes

Blood collected in blood gas syringes

Haemolysis, defined in the published study for the haemolysis s-test as more than 0.5 g per L (50 mg/dL) of free haemoglobin in plasma, was present in 100 samples (7.9% of all samples), as detected by the reference method. This haemolysis cut-off level was used as it is the haemolysis level used by the reference method. In total, 1,270 samples were successfully analysed using both the POC method and the laboratory method. Table 2 and Table 3 (Duhalde et al. 2019) show the diagnostic accuracy of the POC method of haemolysis detection at two different haemoglobin concentration cut-off levels. The POC method identified haemolysed samples (using a cut-off of 0.5 g/L [50 mg/dL] of free haemoglobin in plasma) with a sensitivity of 80% (95% confidence interval [CI]: 70.8% to 87.3%) and a specificity of 99% (95% CI: 98.4% to 99.6%) compared to the reference method. At a cut-off of 1 g/L (100 mg/dL) of free haemoglobin, the POC method identified haemolysed samples with a sensitivity and specificity of 84.8% (95% CI: 71.1% to 93.7%) and 99.9% (95% CI: 99.6% to 100.0%), respectively, compared to the reference method.

Table 2. Diagnostic accuracy of haemolysis (haemolysis cut-off level of 0.5 g/L [50 mg/dL] free haemoglobin in plasma) using POC method in emergency department in Sweden

POC test (n = 1,270)	Reference laboratory test (n = 1,270)		
	Haemolysis present	**Haemolysis absent**	
Haemolysis present	80	10	**PPV (%)**: 88.9 (95% CI [%]: 81.1 to 93.7)
Haemolysis absent	20	1,160	**NPV:** 98.3% (95% CI [%]: 97.5 to 98.9)
	Sensitivity (%): 80.0 (95% CI [%]: 70.8 to 87.3)	**Specificity (%):** 99.2 (95% CI [%]: 98.4 to 99.6)	

CI: confidence interval; POC: point-of-care; PPV: positive predictive value; NPV: negative predictive value

Table 3. Diagnostic accuracy of haemolysis (haemolysis cut-off level of 1 g/L [100 mg/dL] free haemoglobin in plasma) using POC method in emergency department in Sweden

POC test (n=1,270)	Reference laboratory test (n = 1,270)		
	Haemolysis present	**Haemolysis absent**	
Haemolysis present	39	1	**PPV (%):** 97.5 (95% CI [%]: 84.6 to 99.6)
Haemolysis absent	7	1,223	**NPV (%)** 99.4 (95% CI [%]: 98.9 to 99.7)
	Sensitivity (%): 84.8 (95% CI [%]: 71.1 to 93.7)	**Specificity (%):** 99.9 (95% CI [%]: 99.6 to 100.0)	

CI: confidence interval; POC: point-of-care; PPV: positive predictive value; NPV: negative predictive value

One hundred and sixty-four blood samples, where the Helge POC device measured a free haemoglobin value of more than 0.3 g/L (30 mg/dL) (which was considered close to the clinical cut-off level of haemolysis of 0.5g/L [50 mg/dL]), were analysed with more detailed continuous data using the reference method to ensure the POC results and reference results were on the same side of the clinical cut-off. It showed a correlation between the haemolysis levels recorded by the POC device and the laboratory device: correlation coefficient = 0.91 ($p < .05$); Spearman's correlation test correlation coefficient = 0.85 ($p < .0001$) (Duhalde et al. 2019).

Blood collected in test tubes

The unpublished conference poster providing information on a method comparison study of POC haemolysis-detection in vacuum tubes (Helge v-test) also used clinically relevant haemolysis at a level of 0.5 g/L (50 mg/dL) and 1 g/L (100 mg/dL) free haemoglobin. Based on this evidence, it is suggested that the proportion of laboratory-rejected samples would be reduced in those samples tested using the Helge v-test compared to those not pre-tested.

The press release describing the effect on haemolysis detection using Hemcheck's Helge product for test tubes (v-test) reported that the frequency of haemolysed blood samples sent to the central laboratory was 54% lower in those samples tested using the Helge v-test compared to those that were not pre-tested (Hemcheck Sweden AB 2020).

We did not find any published evidence for several of the outcomes listed in the PICO table (Appendix 1): time required for sample analysis; changes in requirement for re-sampling/ability to re-sample using original venepuncture site; patient satisfaction and reduction in anxiety; and changes in resource requirements.

5.2 Ongoing trials

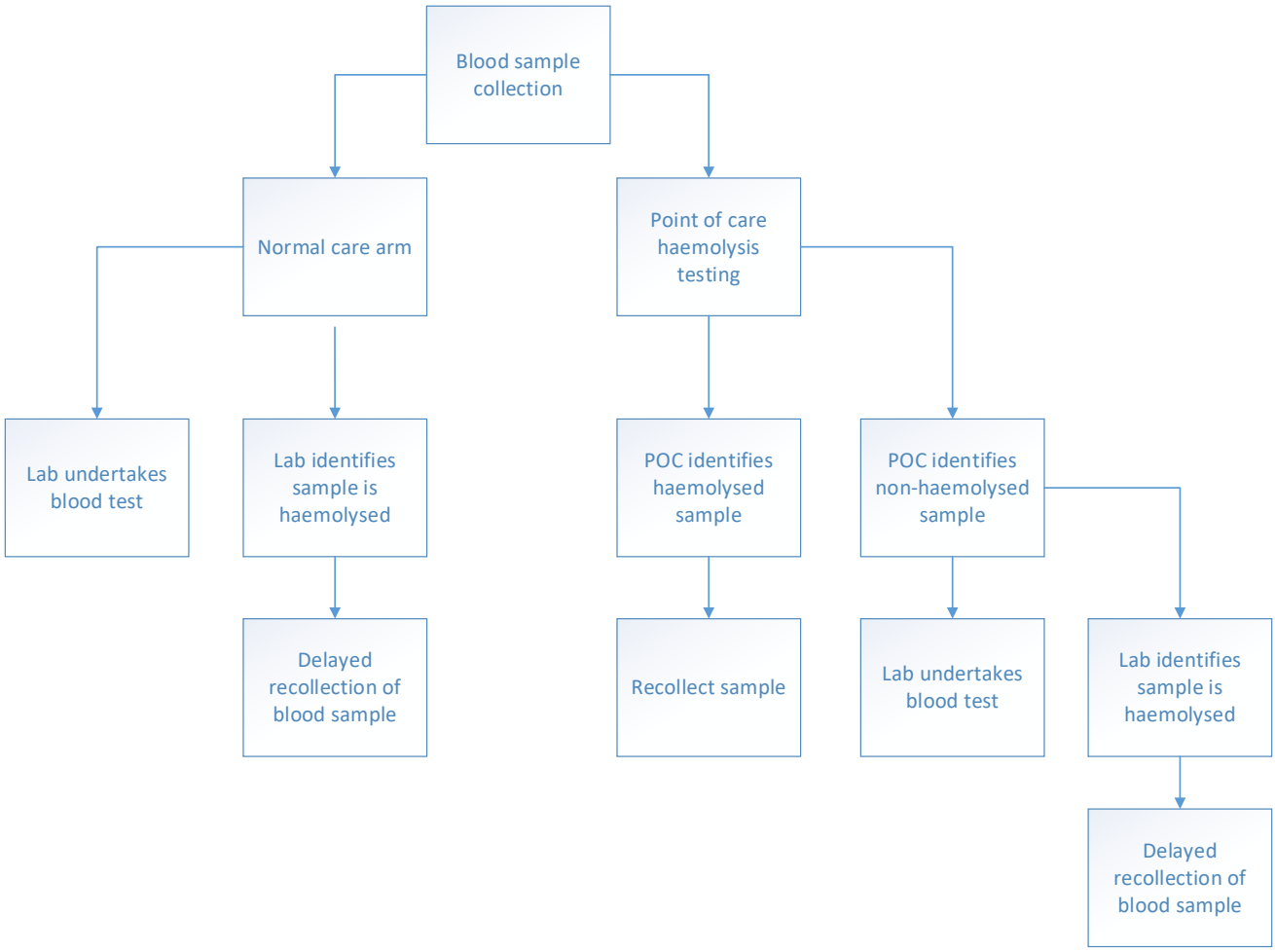
We did not identify any ongoing clinical trials. The Topic Proposer states that they are planning additional clinical trials in live settings at different European hospitals for both the s-test and the v-test.

6. Economic evaluation

Titles and abstracts identified through the systematic literature search were screened for inclusion in the economic evaluation: one paper was included in this analysis (Green 2013). The study submitted by the Topic Proposer was incorporated into the economic approach (Duhalde et al. 2019). The topic proposal included a cost-benefit analysis (CBA) model which will be adapted, alongside the clinical evidence, to form the basis of this analysis. The clinical evidence reported above offers the sensitivity and specificity of the POC haemolysis detection device compared to the reference case laboratory test.

The population for this evaluation is anyone having a blood sample taken in the A&E setting. The perspective of the study is a limited NHS costing approach comparing POC haemolysis with standard care. The analysis takes place over a short period (< 1 year): therefore, discounting is not included. Health outcomes are focused on the financial impact, and the evaluation follows a CBA framework. Effectiveness of the intervention is based on the diagnostic accuracy and subsequent changes to the patient pathway. This CBA is a model-based approach, which uses the decision tree structure to compare the two arms. Costs are reported in 2019 GBP, with prevailing exchange rates being used alongside consumer price index inflation adjustment.

Figure 1. POC haemolysis testing framework



6.1 Economic model

The economic approach taken in this review follows the structure of Figure 1. The intervention arm benefits from the early identification of a haemolysed sample and timely recollection of the sample, this helps to mitigate the issues associated with delayed recollection. The accuracy by which the haemolysed sample can be identified is reported by Duhalde et al. (2019). The economic analysis assumes a clinically important level of haemolysis to be 0.5 g/L (50 mg/dl). The sensitivity and specificity of the POC haemolysis test is 80.00% and 99.20%, respectively. POC testing was shown to offer a positive predictive value of 88.9% and a negative predictive value of 98.3% (Duhalde et al. 2019). For clarity and continuity, the base case analysis will be estimated using a cohort of 1,270 patients, in line with published outcomes.

6.1.1 Device cost

A POC haemolysis device costs approximately £600 per month, and the capacity of the device is assumed to be around 4,000 tests yearly. The reported costs range between £500 and £1,000 per month. Costs associated with v-test consumables are included in the monthly cost. Training and maintenance are included in the monthly cost. A £600 per month cost and a yearly capacity of 4,000 tests offers a cost per test of £1.80 ([600*12]/4000). The process of testing the blood sample using the POC haemolysis approach take approximately seven seconds: this equates to £0.16 in direct labour costs.

6.1.2 Pathway changes

The diagnostic accuracy is offered by Table 2, above. The POC haemolysis test identifies 90 samples to be haemolytic: blood samples are recollected immediately in these cases.

Table 2 presents the accuracy of POC haemolysis as a diagnostic for haemolysis at a 0.5 g/L (50 mg/dL) level. According to the sensitivity, POC haemolysis would lead to 90 samples being recollected, with 20 missed cases of haemolysis and 80 correctly identified samples. Recollection costs of samples following the identification of haemolysis is estimated according to a bottom-up approach. Nurse time is combined with the cost of consumables to reflect the full cost of a recollection.

The reported time to recollect blood is four minutes. A band six nurse cost of £1.40 per patient-related contact minute was included in this analysis. The consumable items required for blood collection amount to a total of £0.38.

An assumption in this economic modelling is that the resampled collection is not haemolysed. This simplification assumption may bias the analysis in favour of the POC haemolysis test as the estimated impact of delayed testing includes observed data and the possibility of subsequent haemolysed samples. This assumption impacts both sides of the analysis as delayed resampling is also assumed to not be haemolysed.

6.1.3 Impact of haemolysed sample

Green (2013) estimates the economic cost of rejected blood samples. Green (2013) follows a methodology which looks to capture the impact of poor blood specimen quality through the identification of its knock-on effects. The impact of a rejected blood sample on the subsequent patient treatment is estimated using clinical data supported by expert opinion. A disparity in the clinical severity of a rejected sample was identified according to hospital setting. Cost estimates are separated into three categories: outpatients, inpatients and critical inpatients.

Costs are estimated according to the additional processes required following the rejected sample. Costs consider blood collection consumables, redraw times, laboratory investigation costs, instrument downtime costs and additional patient treatment costs. The most influential component of the additional costs is that of patient treatment costs: this represents approximately 70% of total costs. Green (2013) reports the additional costs in euros as €107.62 for outpatients, €245.37 for inpatients and €177.98 for critical inpatients. Adjusting the outpatient figure to 2019 GBP offers an estimated cost per haemolysed sample of £106.31. Current prices were estimated the prevailing exchange rate and the consumer price index inflation rate.

6.2 Base case model

The base case CBA compared the additional costs associated with haemolysed blood tests. The standard treatment costs following the test are not included. The limited scope of this analysis can be broadly summarised to be the comparison between the standard care arm, which has higher levels of delayed sample collection, and the intervention of POC haemolysis, which has a higher upfront cost but reduces the number of haemolysed samples which are sent to the centralised laboratory for testing. The model cohort of 1,270 are presented below in Table 4.

Table 4. POC haemolysis: base case total costs comparison

POC test (n = 1,270)	POC haemolysis	Standard care	Difference
Device cost	£2,286		£2,286
POC Haemolysis collection costs	£207		£207
Resampling costs	£538		£538
Cost of delayed resampling	£2,126	£10,613	-£8,487
Total cost	£5,158	£10,631	-£5,473
POC: point-of-care			

The base case model suggests that the POC haemolysis approach is associated with a reduction in costs of around £5,473. Scaling the outcomes to reflect a single blood test model offers a saving of around £4 per test.

6.2.1 Sensitivity analysis

The base case analysis incorporates a significant amount of uncertainty. A fundamental uncertainty of the approach is chosen threshold level of haemolysis at which a test would need to be resampled. Duhalde et al. (2019) reported diagnostic accuracy for the haemolysis threshold of 1 g/L (100 mg/dL): this uses a reference test with the same cut-off level. The 1 g/L (100 mg/dL) haemolysis approach has a prevalence level of 3.62%, sensitivity of 84.8% and specificity of 99.9%. Table 5 presents the CBA results for 1 g/L (100 mg/dL).

Table 5. Comparative costs of POC haemolysis at 1 g/L (100 mg/dL) threshold

POC test (n = 1,270)	POC haemolysis	Standard care	Difference
Device cost	£2,286		£2,286
POC Haemolysis collection costs	£207		£207
Resampling costs	£240		£240
Cost of delayed resampling	£743	£4,890	-£4,147
Total cost	£3,477	£4,890	-£1,413
POC: point-of-care			

The approach suggests that POC testing is associated with a reduction in costs of £1,413 for the cohort: this equates to slightly more than £1 per test taken. The lower prevalence rate is associated with a reduction in cost savings. The 1 g/L (100 mg/dL) threshold test has a higher sensitivity and specificity, which would partially offset the reduced cost savings related to the lower prevalence.

6.2.2 Resampling cost setting

There is uncertainty surrounding the figure used to reflect the cost of a delayed sample, this is due to the age of the publication and the generalisability of the findings to the NHS context in Wales. The base case approach uses an A&E level of cost. Substituting the alternative costs identified in Green (2013) offers the findings reported in Table 6: these estimates are assessed for the 0.5 g/L (50 mg/dL) and 1 g/L (100 mg/dL) cases.

Table 6. One-way sensitivity analysis: resample cost setting

Resampling cost setting	Resampling cost	0.5 g/L (50 mg/dL)	1 g/L (100 mg/dL)
A&E (base case)	**£106**	**-£5,473**	**-£1,413**
Inpatients	£242	-£16,359	-£6,720
Inpatients (critical)	£176	-£11,033	-£4,124
A&E: Accident and Emergency; g/L: grams per litre; mg/dL: milligrams per decilitre			

At the prevailing prevalence rates, the threshold cost of a delayed resampled test is £38 and £70 for 0.5 g/L (50 mg/dL) and 1 g/L (100 mg/dL), respectively.

6.2.3 Threshold analysis

Prevalence has a high level of impact on the overall cost impact of the intervention. Varying the prevalence level for each of the two haemolysis level can offer an important insight into the scale of influence. Each haemolysis level is observed across a 1% to 5% prevalence level and reported in Table 7 (n = 1,270). The break-even prevalence for 0.5 g/L (50 mg/dL) and 1 g/L (100 mg/dL) is 2.51% and 2.31%, respectively.

Table 7. One-way sensitivity analysis: prevalence level

Prevalence level	0.5 g/L (50 mg/dL)	1 g/L (100 mg/dL)
1%	£1,538	£1,420
2%	£518	£340
3%	-£502	-£741
4%	-£1,522	-£1,821
5%	-£2,542	-£2,902
g/L: grams per litre; mg/dL: milligrams per decilitre		

6.2.4 Two-way sensitivity analysis

To characterise the uncertainty inherent within the economic model, a two-way sensitivity analysis was undertaken. The two most prominent areas of influence and uncertainty, namely prevalence and the cost of a delayed sample, are included in a repeated estimation that aids in identifying their joint influence. The range of prevalence used for the model is from 1% to 12%. The range of cost estimates used in the model range from £30 to £210. The base case estimates are included alongside chosen integer estimates, and outcomes are reported in Table 8 below.

Table 8. Two-way sensitivity analysis: cost or delayed resampling and prevalence rate

Cost of delayed resampling (n=1,270)								
Prevalence level	£30	£60	£90	£106.31	£120	£150	£180	£210
1.00%	2,314	2,009	1,704	1,538	1,399	1,094	790	485
2.00%	2,069	1,459	850	518	240	-370	-979	-1,589
3.00%	1,824	910	-5	-502	-919	-1,833	-2,748	-3,662
4.00%	1,579	360	-859	-1,522	-2,078	-3,297	-4,517	-5,736
5.00%	1,335	-189	-1,713	-2,542	-3,237	-4,761	-6,285	-7,809
6.00%	1,090	-739	-2,568	-3,562	-4,396	-6,225	-8,054	-9,883
7.00%	845	-1,288	-3,422	-4,582	-5,556	-7,689	-9,823	-11,956
7.87%	632	-1,766	-4,165	-5,469	-6,564	-8,963	-11,362	-13,760
8.00%	601	-1,838	-4,276	-5,602	-6,715	-9,153	-11,591	-14,030
9.00%	356	-2,387	-5,131	-6,622	-7,874	-10,617	-13,360	-16,103
10.00%	111	-2,937	-5,985	-7,642	-9,033	-12,081	-15,129	-18,177
11.00%	-134	-3,486	-6,839	-8,662	-10,192	-13,545	-16,898	-20,250
12.00%	-378	-4,036	-7,694	-9,682	-11,351	-15,009	-18,666	-22,324

The two-way sensitivity analysis highlights the outcomes in green where there is a cost saving and red where the intervention is more costly than standard care. Savings reduce with lower prevalence levels and lower costs associated with delayed resampling.

7. Organisational issues

The Welsh Scientific Advisory Committee (2017) published a policy on POCT in Wales (this is not specific to haemolysis POCT). It states that the POCT department of each health board should provide advice on how to implement and manage the POCT service. Use of POC haemolysis detection will result in potential training needs for clinical staff, as well as added resources needed for the maintenance of the POCT equipment.

8. Patient issues

None of the studies identified included any information on patients' perspectives or experiences of POC haemolysis detection. Clinical expert input suggested that some patient blood samples are at increased risk of haemolysis due to certain medical conditions. Clinical expert feedback also stated that POCT for haemolysis could potentially enhance patient care by reducing time spent in A&E.

9. Conclusions

The evidence identified showed that that the Helge haemolysis POCT device (using the s-test only) has the potential to detect haemolysis with a sensitivity of 80% and a specificity

of 99%, at a haemoglobin concentration cut-off of 0.5 g/L (50 mg/dL), and a sensitivity of 84.8% and specificity of 99.9%, at a haemoglobin concentration cut-off of 1 g/L (100 mg/dL). One unpublished conference poster showed that that the proportion of laboratory-rejected samples would be reduced in those samples tested using the Helge v-test compared to those not pre-tested. The studies was conducted in the Swedish healthcare system, which differs from Welsh practice.

No evidence was identified about how POC haemolysis detection influences the time required for sample analysis, changes in requirement for re-sampling/ability to re-sample using the original puncture site, or patient satisfaction.

The CBA suggests that POC haemolysis testing is associated with a net cost reduction. The range of sensitivity analyses highlight prevalence and the cost of a delayed resampling as highly impactful. Given the uncertainty surrounding the highly influential figures, the conclusion should be carefully and cautiously considered.

10. Contributors

This topic was proposed by Joen Averstad, CEO, Hemcheck Sweden AB.

The HTW staff and contract researchers involved in writing this report were:

- J Washington – literature search
- J Williams – clinical author
- T Winfield – health economics author and lead author
- D Jarrom – editor
- S McAllister – project management
- A Evans – patient and public involvement author

The HTW Assessment Group advised on methodology throughout the scoping and development of the report.

A range of clinical experts from the UK provided material and commented on a draft of this report. Their views were documented and have been actioned accordingly. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control, and the views expressed are those of Health Technology Wales.

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Appendix 1. PICO framework

Research Question	What is the clinical and cost effectiveness of using point-of-care testing to detect haemolysis in blood samples?

	Inclusion criteria	**Exclusion criteria**
Population	Patients undergoing blood testing in secondary care Where possible, we will conduct a subgroup analysis according to specific settings, such as, but not limited to: ITU Emergency care Outpatients Paediatrics	Blood testing conducted outside of the secondary care setting
Intervention	Point-of-care haemolysis testing	
Comparison/ Comparators	Standard centralised (laboratory-based) blood testing processes	
Outcome measures	Diagnostic accuracy Reduction in haemolysed samples being sent for blood testing Time required for sample analysis Changes in requirement for re-sampling/ability to re-sample using original venepuncture site Patient satisfaction: reduction in anxiety Changes in resource requirements	
Study design	Studies of diagnostic accuracy Any form of economic evaluation Interventional studies of any design (with or without a control group)	
Search limits	No date limits Studies in English language only	

Appendix 2. PRISMA flow diagram outlining selection of papers for clinical and cost effectiveness (Evidence to September 2020)